

Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

1. (previously presented) A vector system for selectively packaging a replication defective adenovirus nucleic acid sequence in an adenovirus capsid based on adenovirus serotype, the vector system comprising:

- (a) a first adenovirus nucleic acid sequence comprising:
  - (i) 5' and 3' adenovirus inverted terminal repeats (ITRs);
  - (ii) a first adenovirus serotype-specific cis-acting packaging sequence; and
  - (iii) a heterologous nucleic acid operably linked to a transcriptional control sequence;

wherein the first adenovirus nucleic acid sequence comprises a defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, penton gene, fiber gene, hexon gene, or a combination thereof, and wherein the first adenovirus nucleic acid fails to encode a 52/55 kDa trans-acting protein specific for the first cis-acting packaging sequence;

- (b) a second adenovirus nucleic acid sequence comprising:
  - (i) 5' and 3' adenovirus ITRs;
  - (ii) a second adenovirus serotype-specific cis-acting packaging sequence; and

wherein the second adenovirus nucleic acid sequence complements the defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, penton gene, fiber gene, hexon gene, or a combination thereof of the first adenovirus nucleic acid sequence, and wherein the second adenovirus nucleic acid fails to encode a 52/55 kDa trans acting protein specific for the second cis-acting packing sequence;

(c) an adenovirus replication competent host cell comprising a nucleic acid sequence encoding an adenovirus 52/55 kDa trans-acting protein that supports packaging of the first adenovirus nucleic acid sequence and fails to support packaging of the second adenovirus nucleic acid sequence,

wherein the replication defective adenovirus comprises the first adenovirus nucleic acid sequence.

2. (previously presented) The vector system of claim 1, wherein the adenovirus capsid and 52/55 kDa protein are from human adenovirus and wherein the first and second adenovirus nucleic acid sequences are from human adenovirus.

3. (previously presented) The vector system of claim 1, wherein the first and second adenovirus serotype-specific cis-acting packaging sequences are selected from the group consisting of adenovirus type 2 (Ad2), adenovirus type 5 (Ad5), adenovirus type 7 (Ad7), adenovirus type 12 (Ad12), adenovirus type 17 (Ad17), and adenovirus type 40 (Ad40) packaging sequences, and wherein the first serotype-specific cis-acting packaging sequence is from a different serotype than the second adenovirus serotype-specific cis-acting packaging sequence.

4. (previously presented) The vector system of claim 3, wherein the first adenovirus serotype-specific cis-acting packaging sequence is from adenovirus type 5 and the second adenovirus serotype-specific cis-acting packaging sequence is from adenovirus type 7.

5. (previously presented) The vector system of claim 3, wherein the first adenovirus serotype-specific cis-acting packaging sequence is from adenovirus type 7 and the second adenovirus serotype-specific cis-acting packaging sequence is from adenovirus type 5.

6-9. (canceled)

10. (previously presented) The vector system of claim 1, wherein the failure to encode a functional 52/55 kDa trans-acting protein is due to a mutation in the sequence encoding the protein.

11. (original) The vector system of claim 10, wherein the mutation is a missense mutation, a point mutation, a frameshift mutation or a deletion mutation.

12. (canceled)

13. (currently amended) The vector system of claim 1, wherein the nucleic acid sequence encoding an adenovirus 52/55 kDa trans-acting protein that supports packaging of the first adenovirus nucleic acid sequence is encoded by a nucleic acid sequence functionally-associated with the genome of ~~an~~ the adenovirus replication competent host cell containing the vector system.

14. (original) The vector system of claim 13, wherein the adenovirus replication competent host cell is a 293 cell line.

15-16. (canceled)

17. (previously presented) A vector system for selectively packaging a replication defective adenovirus nucleic acid sequence in an adenovirus capsid based on adenovirus serotype, the vector system comprising:

- (a) a first adenovirus nucleic acid sequence comprising:
    - (i) 5' and 3' adenovirus ITRs;
    - (ii) a first adenovirus serotype-specific cis-acting packaging sequence; and
    - (iii) a heterologous nucleic acid operably linked to a transcriptional control sequence;

wherein the first adenovirus nucleic acid sequence comprises a defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, penton gene, fiber gene, hexon gene, or a combination thereof, and wherein the first adenovirus nucleic acid fails to encode a 52/55 kDa trans-acting protein specific for the first cis-acting packaging sequence;
  - (b) a second adenovirus nucleic acid sequence comprising:
    - (i) 5' and 3' adenovirus ITRs;
    - (ii) a second adenovirus serotype-specific cis-acting packaging sequence;
    - (iii) a nucleic acid sequence encoding an adenovirus 52/55 kDa trans-acting protein that supports packaging of the first adenovirus nucleic acid sequence and fails to support packaging of the second adenovirus nucleic acid sequence;

wherein the second adenovirus nucleic acid sequence complements the defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, penton gene, fiber gene, hexon gene, or a combination thereof of the first adenovirus nucleic acid sequence; and
  - (c) an adenovirus replication competent host cell;
- wherein the replication defective adenovirus comprises the first adenovirus nucleic acid sequence.

18. (canceled)

19. (canceled)

20. (currently amended) A vector comprising a replication defective adenovirus sequence comprising:

(a) a first adenovirus serotype-specific cis-acting packaging sequence;  
and

(b) a nucleic acid sequence encoding a functional ~~second~~ adenovirus serotype-specific 52/55 kDa protein, wherein said protein is specific for a second adenovirus serotype specific cis-acting packaging sequence and is not specific for the first adenovirus serotype-specific cis acting packaging sequence,

wherein the replication defective adenovirus sequence comprises a defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, penton gene, fiber gene, hexon gene, or a combination thereof.

21. (previously presented) The vector of claim 20, further comprising at least one adenoviral nucleic acid sequence needed to produce an adenoviral capsid.

22. (previously presented) The vector of claim 21, further comprising sufficient adenoviral nucleic acid sequence to encode a complete adenoviral capsid when the vector is expressed in an adenovirus replication-competent host cell.

23. (currently amended) The vector of claim 20, wherein the first adenovirus serotype specific cis-acting packaging sequence and second adenovirus serotype-specific sequence are selected from an adenovirus from the group consisting of adenovirus type 2 (Ad2), adenovirus type 5 (Ad5), adenovirus type 7 (Ad7), adenovirus type 12 (Ad12),

adenovirus type 17 (Ad17), and adenovirus type 40), and wherein the first serotype-specific cis-acting packaging sequence is from an adenovirus of a different serotype than the second adenovirus serotype-specific cis-acting packaging sequence.

24. (currently amended) The vector of claim 23, wherein the first adenovirus serotype sequence is from adenovirus type 5 and the second adenovirus serotype sequence is from adenovirus type 7.

25. (currently amended) The vector of claim 23, wherein the first adenovirus serotype sequence is from adenovirus type 7 and the second adenovirus serotype sequence is from adenovirus type 5.

26. (previously presented) A transformed or isolated infected cell comprising the vector of claim 20.

27. (currently amended) A kit useful for producing ~~adenovirus~~ encapsidated adenovirus replication defective nucleic acid sequences, the kit comprising: ~~comprising~~

(a) a container containing a first adenovirus nucleic acid sequence comprising:

- (i) 5' and 3' adenovirus inverted terminal repeats (ITRs);
- (ii) a first adenovirus serotype-specific cis-acting packaging sequence; and
- (iii) a heterologous nucleic acid operably linked to a transcriptional control sequence;

wherein the first adenovirus nucleic acid sequence comprises a defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, penton gene, fiber gene, hexon gene, or a

combination thereof, and wherein the first adenovirus nucleic acid fails to encode a 52/55 kDa trans-acting protein specific for the first cis-acting packing sequence;

(b) a container containing a second adenovirus nucleic acid sequence comprising:

(i) 5' and 3' adenovirus ITRs;

(ii) a second adenovirus serotype-specific cis-acting packaging sequence; and wherein the second adenovirus nucleic acid sequence complements the defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, penton gene, fiber gene, hexon gene, or a combination thereof of the first adenovirus nucleic acid sequence, and wherein the second adenovirus nucleic acid fails to encode a 52/55 kDa trans acting protein specific for the second cis-acting packing sequence;

(c) a container containing an adenovirus replication competent host cell comprising a nucleic acid sequence encoding an adenovirus 52/55 kDa trans-acting protein that supports packaging of the first adenovirus nucleic acid sequence and fails to support packaging of the second adenovirus nucleic acid sequence,

wherein the replication defective adenovirus comprises the first adenovirus nucleic acid sequence.

28-30. (canceled)

31. (currently amended) A method of producing an encapsidated a replication defective ~~encapsidated~~ adenovirus vector, comprising:

(a) transforming or infecting ~~into an~~ adenovirus replication competent host cells with

- (i) a first adenovirus nucleic acid sequence comprising:
  - 5' and 3' adenovirus inverted terminal repeats (ITRs);
  - a first adenovirus serotype-specific cis-acting packaging sequence; and
  - a heterologous gene operably linked to a transcriptional control sequence,wherein the first adenovirus nucleic acid sequence comprises a defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, penton gene, fiber gene, hexon gene, or a combination thereof, and wherein the first adenovirus nucleic acid fails to encode a 52/55 kDa trans-acting protein specific for the first cis-acting packing sequence;
- (ii) a second adenovirus nucleic acid sequence comprising:
  - 5' and 3' adenovirus ITRs;
  - a second adenovirus serotype-specific cis-acting packaging sequence,wherein the second adenovirus nucleic acid sequence complements the defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, penton gene, fiber gene, hexon gene, or a combination thereof of the first adenovirus nucleic acid sequence, and wherein the second adenovirus nucleic acid fails to encode a 52/55 kDa protein specific for the second adenovirus serotype-specific cis-acting packaging sequence; and
- (iii) a nucleic acid sequence encoding an adenovirus 52/55 kDa protein specific for a the first adenovirus serotype-specific cis-acting packaging sequence; and



(b) culturing the host cells under conditions where the first adenovirus sequence is encapsidated to produce a replication defective adenovirus vector.

32. (currently amended) A method of producing an encapsidated a replication defective ~~encapsidated~~ adenovirus vector, comprising:

(a) transforming or infecting ~~into an~~ adenovirus replication competent host cells with a first and second adenovirus nucleic acid ~~replication defective~~ sequences, wherein the cell comprises a nucleic acid sequence encoding an adenovirus 52/55 kDa trans-acting protein that supports packaging of a the first adenovirus nucleic acid sequence and fails to support packaging of a the second adenovirus nucleic acid sequence, and wherein

(i) the first adenovirus nucleic acid sequence comprises:

5' and 3' adenovirus inverted terminal repeats

(ITRs);

a first adenovirus serotype-specific cis-acting packaging sequence; and

a heterologous gene operably linked to a transcriptional control sequence,

wherein the first adenovirus nucleic acid sequence comprises a defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, penton gene, fiber gene, hexon gene, or a combination thereof, and wherein the first adenovirus nucleic acid fails to encode a 52/55 kDa trans-acting protein specific for the first cis-acting packing sequence;

(ii) the second adenovirus nucleic acid sequence comprises:

5' and 3' adenovirus ITRs;

a second adenovirus serotype-specific cis-acting packaging sequence,

wherein the second adenovirus nucleic acid sequence complements the defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, penton gene, fiber gene, hexon gene, or a combination thereof of the first adenovirus nucleic acid sequence, and wherein the second adenovirus nucleic acid fails to encode a 52/55 kDa trans acting protein specific for the second adenovirus serotype-specific cis-acting packaging sequence; and

(b) culturing the cells under conditions where the first adenovirus sequence is encapsidated to produce a replication defective adenovirus vector.

33. (currently amended) A method of producing an encapsidated a replication defective ~~encapsidated~~ adenovirus vector, comprising the following steps:

(a) transforming or infecting ~~a first and second~~ adenovirus replication ~~defective sequences into an adenovirus replication~~ competent host cells with a first and second adenovirus replication defective sequence, wherein

(i) the first adenovirus nucleic acid sequence comprises:

5' and 3' adenovirus inverted terminal repeats (ITRs);

a first adenovirus serotype-specific cis-acting packaging sequence;

a heterologous gene operably linked to a transcriptional control sequence; and

a nucleic acid sequence encoding an adenovirus 52/55 kDa protein specific for the first adenovirus serotype-specific cis-acting packaging sequence,

wherein the first adenovirus nucleic acid sequence comprises a defective or modified adenovirus E1 gene, E2A gene,

E2B gene, E3 gene, E4 gene, E4 promoter, penton gene, fiber gene, hexon gene, or a combination thereof; and

(ii) the second adenovirus nucleic acid sequence comprises:

5' and 3' adenovirus ITRs;

a second adenovirus serotype-specific cis-acting packaging sequence,

wherein the second adenovirus nucleic acid sequence complements the defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, penton gene, fiber gene, hexon gene, or a combination thereof of the first adenovirus nucleic acid sequence, and wherein the second adenovirus nucleic acid fails to encode a 52/55 kDa trans acting protein specific for the second adenovirus serotype-specific cis-acting packaging sequence; and

(b) culturing the cells under conditions where the first adenovirus sequence is encapsidated to produce a replication defective adenovirus vector.

34. (canceled)

35. (previously presented) A vector for selectively packaging replication defective nucleic acid sequences in adenovirus capsids, the vector comprising:

(a) a replication defective adenovirus sequence comprising an adenovirus serotype 7 (Ad7) cis-acting packaging sequence;

(b) a nucleic acid sequence encoding an adenovirus serotype 5 (Ad5) 52/55 kDa protein; and

(c) an adenoviral nucleic acid sequence that encodes a viral capsid and fails to encode or produce an adenovirus 7 serotype 52/55 kDa trans-acting protein.

36-39. (canceled)

40. (previously presented) A cell for selectively packaging a replication defective adenovirus nucleic acid sequence in an adenovirus capsid, the cell comprising:

- (a) a first adenovirus nucleic acid sequence comprising:
  - (i) 5' and 3' adenovirus inverted terminal repeats (ITRs);
  - (ii) a first adenovirus serotype-specific cis-acting packaging sequence; and
  - (iii) a heterologous nucleic acid operably linked to a transcriptional control sequence,

wherein the first adenovirus nucleic acid sequence comprises a defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, penton gene, fiber gene, hexon gene, or a combination thereof, and wherein the first adenovirus nucleic acid fails to encode a 52/55 kDa trans-acting protein specific for the first cis-acting packaging sequence;

- (b) a second adenovirus nucleic acid sequence comprising:
  - (i) 5' and 3' adenovirus ITRs;
  - (ii) a second adenovirus serotype-specific cis-acting packaging sequence,

wherein the second adenovirus nucleic acid sequence complements the defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, penton gene, fiber gene, hexon gene, or a combination thereof of the first adenovirus nucleic acid sequence, and wherein the second adenovirus nucleic acid fails to encode a 52/55 kDa trans acting protein specific for the second adenovirus serotype-specific cis-acting packaging sequence; and

(c) a nucleic acid sequence encoding an adenovirus 52/55 kDa trans-acting protein specific for the first adenovirus serotype-specific cis-acting packaging sequence,

wherein the replication defective adenovirus comprises the first adenovirus nucleic acid sequence.

41. (previously presented) A cell line for selectively packaging a replication defective adenovirus nucleic acid sequence in an adenovirus capsid, the cell line comprising:

(a) a first adenovirus nucleic acid sequence comprising:

(i) 5' and 3' adenovirus inverted terminal repeats (ITRs);

(ii) a first adenovirus serotype-specific cis-acting packaging sequence; and

(iii) a heterologous nucleic acid operably linked to a transcriptional control sequence,

wherein the first adenovirus nucleic acid sequence comprises a defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, penton gene, fiber gene, hexon gene, or a combination thereof, and wherein the first adenovirus nucleic acid fails to encode a 52/55 kDa trans-acting protein specific for the first cis-acting packaging sequence;

(b) a second adenovirus nucleic acid sequence comprising:

(i) 5' and 3' adenovirus ITRs;

(ii) a second adenovirus serotype-specific cis-acting packaging sequence;

(iii) a nucleic acid sequence encoding an adenovirus 52/55 kDa trans-acting protein that supports packaging of the first adenovirus nucleic

acid sequence and fails to support packaging of the second adenovirus nucleic acid sequence,

wherein the second adenovirus nucleic acid sequence complements the defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, penton gene, fiber gene, or a combination thereof of the first adenovirus nucleic acid sequence,

wherein the replication defective adenovirus comprises the first adenovirus nucleic acid sequence.

42. (canceled)

43. (currently amended) A kit useful for producing ~~adenovirus~~ encapsidated adenovirus replication defective nucleic acid sequences, the kit comprising:

- (a) a first adenovirus nucleic acid sequence comprising:
  - (i) 5' and 3' adenovirus ITRs;
  - (ii) a first adenovirus serotype-specific cis-acting packaging sequence; and
  - (iii) a heterologous nucleic acid operably linked to a transcriptional control sequence;

wherein the first adenovirus nucleic acid sequence comprises a defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, penton gene, fiber gene, hexon gene, or a combination thereof, and wherein the first adenovirus nucleic acid fails to encode a 52/55 kDa trans-acting protein specific for the first cis-acting packaging sequence;

- (b) a second adenovirus nucleic acid sequence comprising:
  - (i) 5' and 3' adenovirus ITRs;

(ii) a second adenovirus serotype-specific cis-acting packaging sequence;

(iii) a nucleic acid sequence encoding an adenovirus 52/55 kDa trans-acting protein that supports packaging of the first adenovirus nucleic acid sequence and fails to support packaging of the second adenovirus nucleic acid sequence;

wherein the second adenovirus nucleic acid sequence complements the defective or modified adenovirus E1 gene, E2A gene, E2B gene, E3 gene, E4 gene, E4 promoter, penton gene, fiber gene, hexon gene, or a combination thereof of the first adenovirus nucleic acid sequence; and

(c) an adenovirus replication competent host cell;

wherein the replication defective adenovirus comprises the first adenovirus nucleic acid sequence.